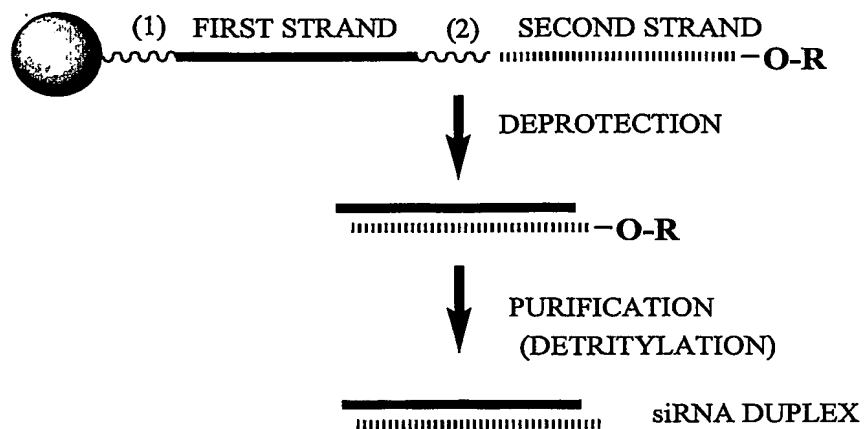


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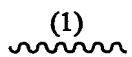
Figure 1

= SOLID SUPPORT

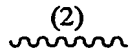
R = TERMINAL PROTECTING GROUP

FOR EXAMPLE:

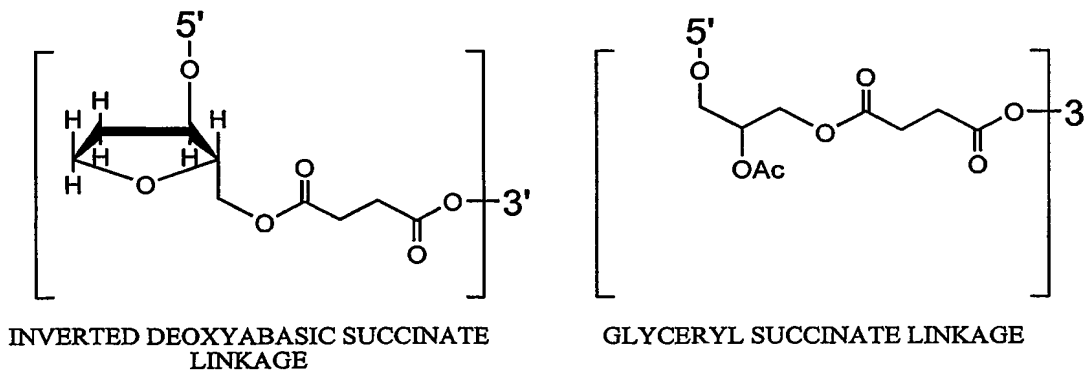
DIMETHOXYTRITYL (DMT)



= CLEAVABLE LINKER

(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
INVERTED DEOXYABASIC SUCCINATE)

= CLEAVABLE LINKER

(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
INVERTED DEOXYABASIC SUCCINATE)

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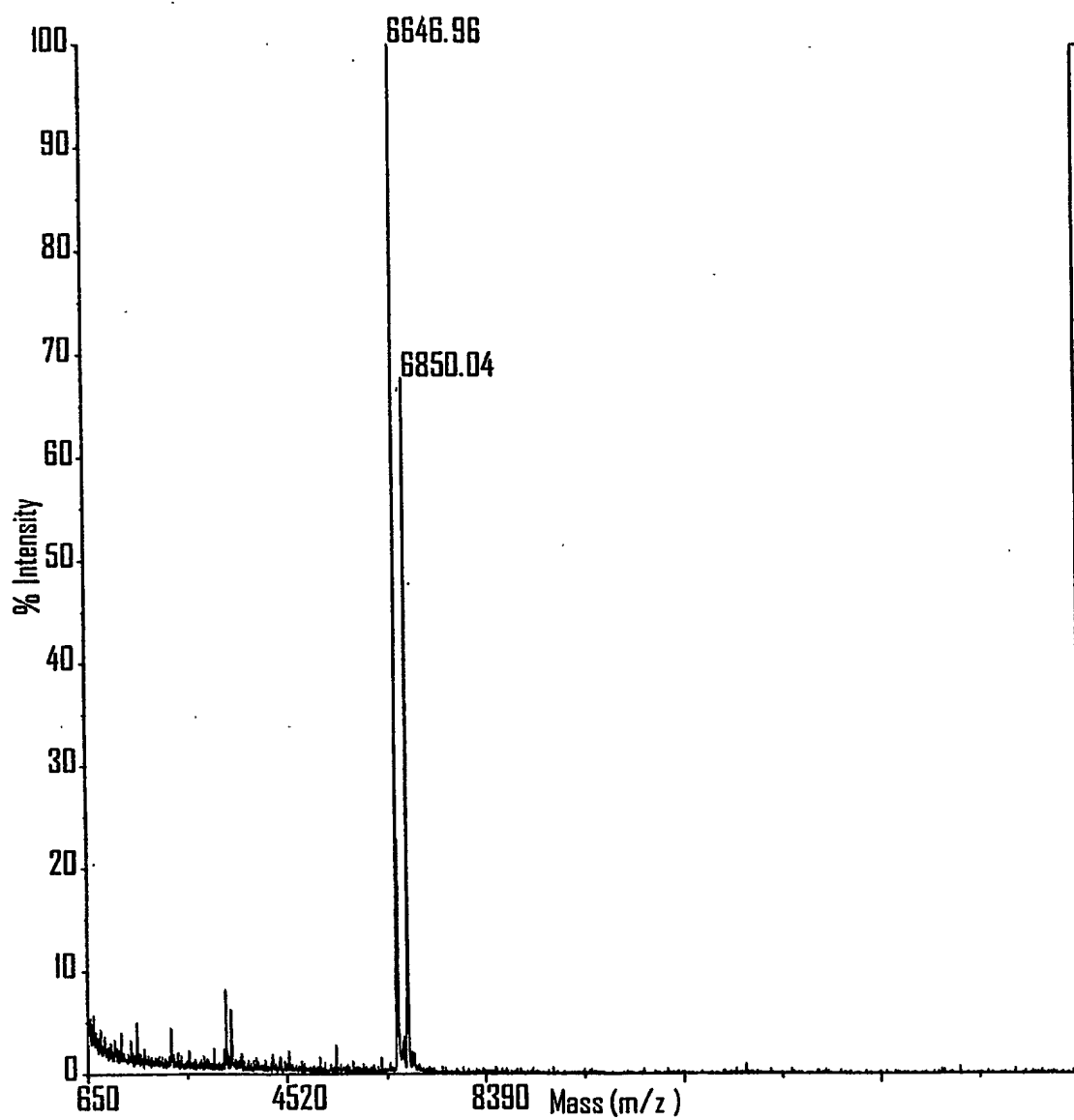
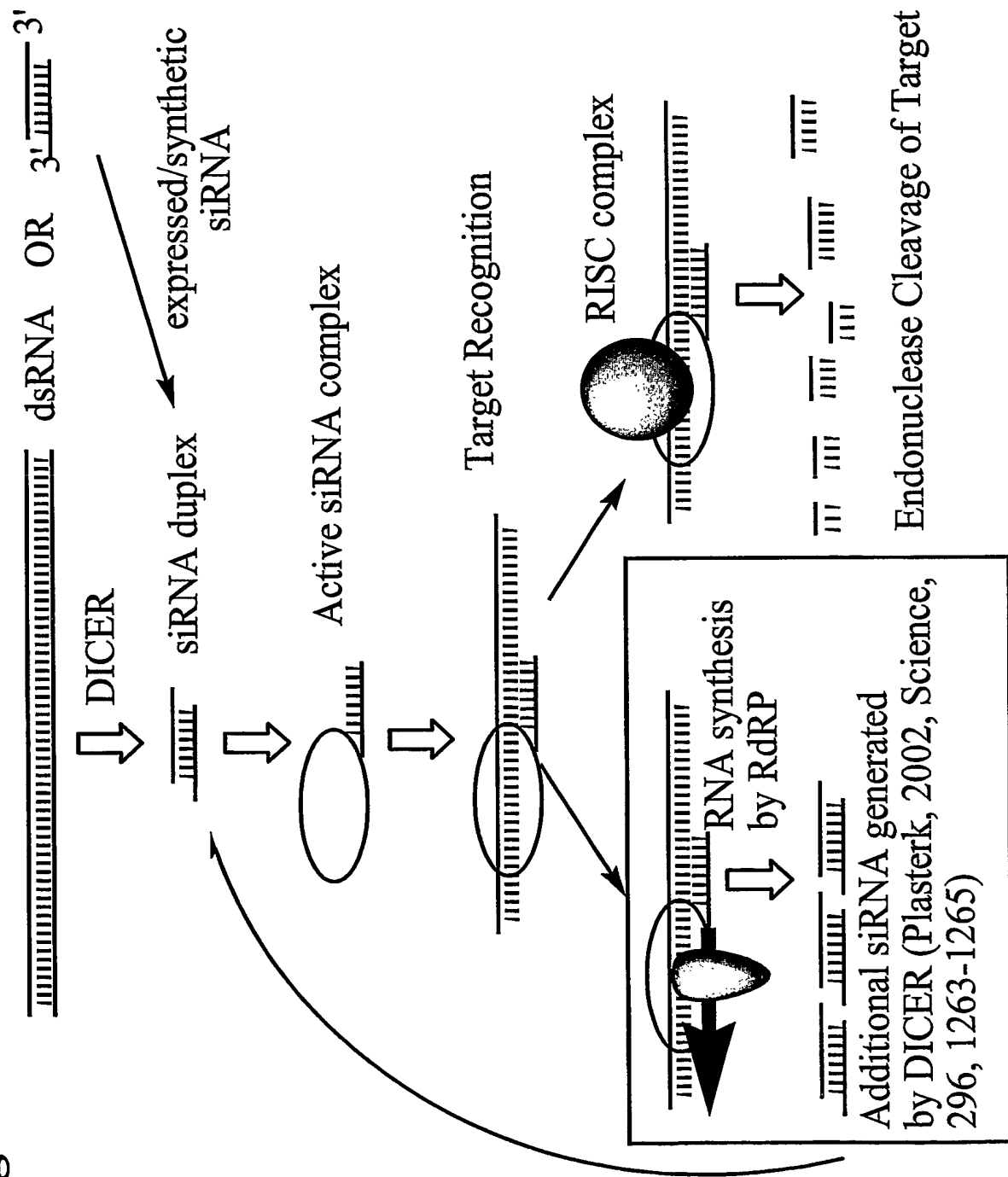
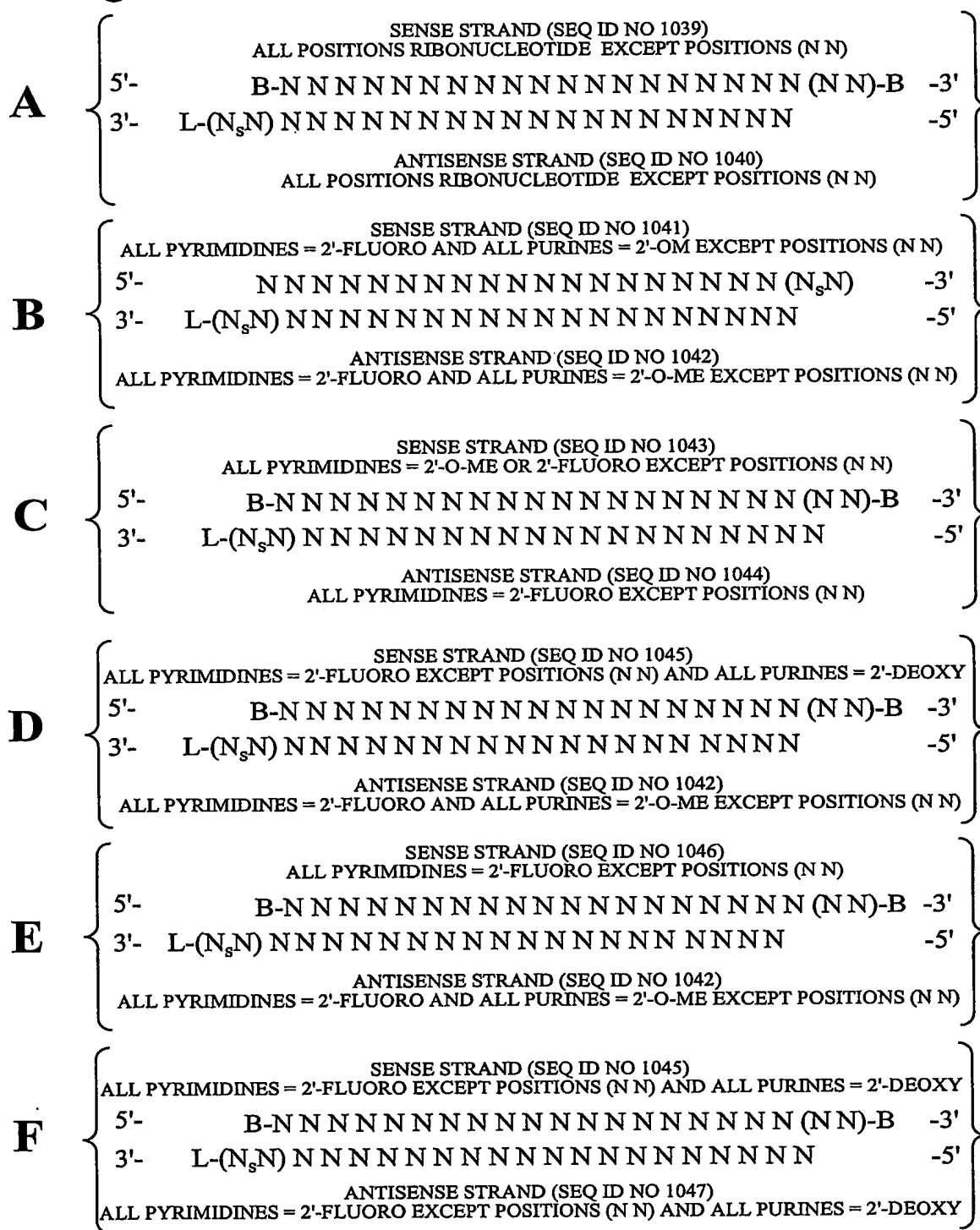
Figure 2

Figure 3

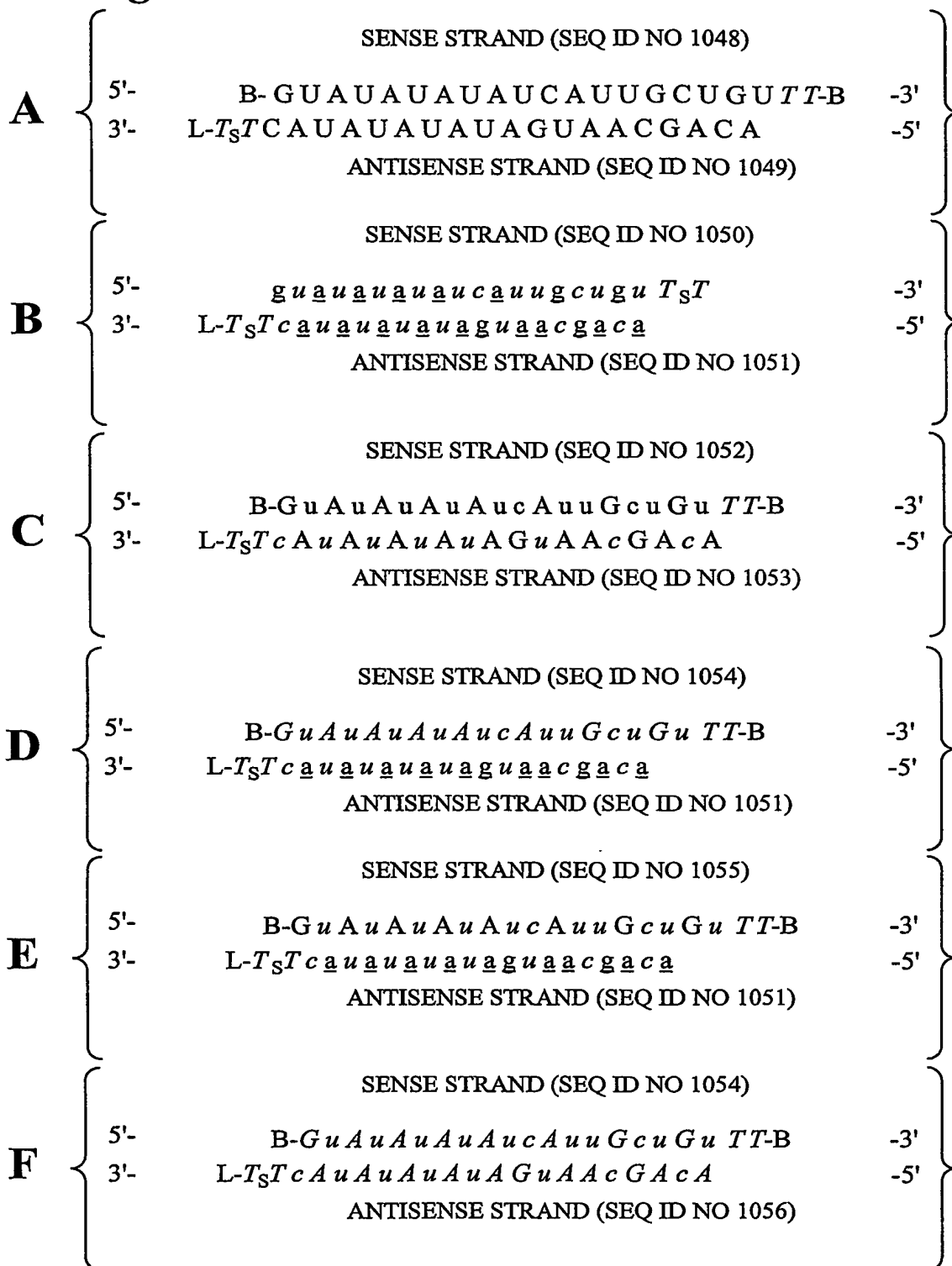


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Figure 4

POSITIONS (NN) CAN COMPRISE ANY NUCLEOTIDE, SUCH AS DEOXYNUCLEOTIDES (eg. THYMIDINE) OR UNIVERSAL BASES
 B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE OR OTHER TERMINAL CAP THAT IS OPTIONALLY PRESENT
 L = GLYCERYL MOIETY THAT IS OPTIONALLY PRESENT
 S = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE THAT IS OPTIONALLY ABSENT

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Figure 5

lower case = 2'-O-Methyl or 2'-deoxy-2'-fluoro

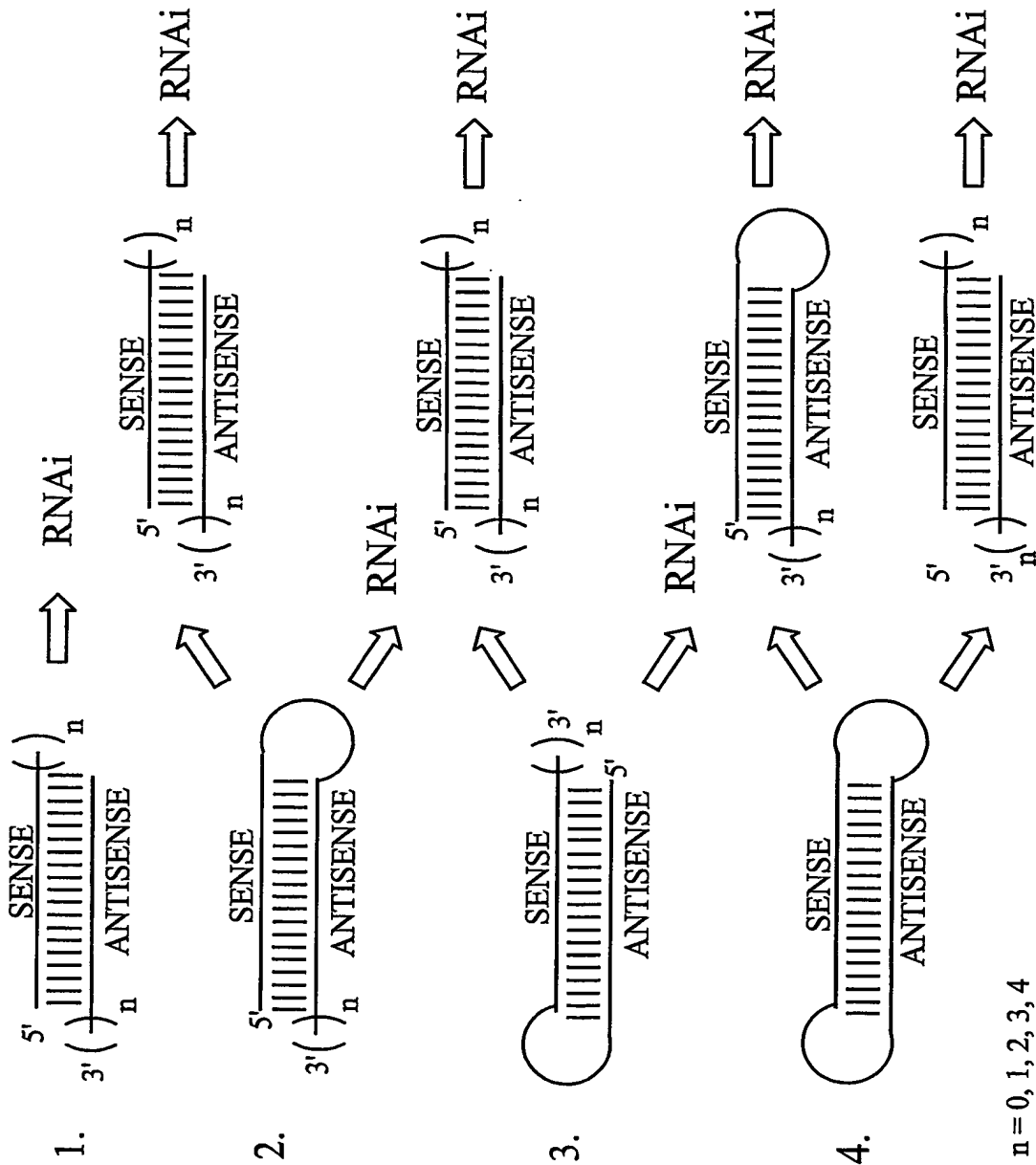
italic lower case = 2'-deoxy-2'-fluorounderline = 2'-O-methyl*ITALIC UPPER CASE* = DEOXY

B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE OR OTHER TERMINAL CAP THAT IS OPTIONALLY PRESENT

L = GLYCERYL MOIETY OPTIONALLY PRESENT

S = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE THAT IS OPTIONALLY ABSENT

Figure 6



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Figure 9: Target site Selection using siRNA

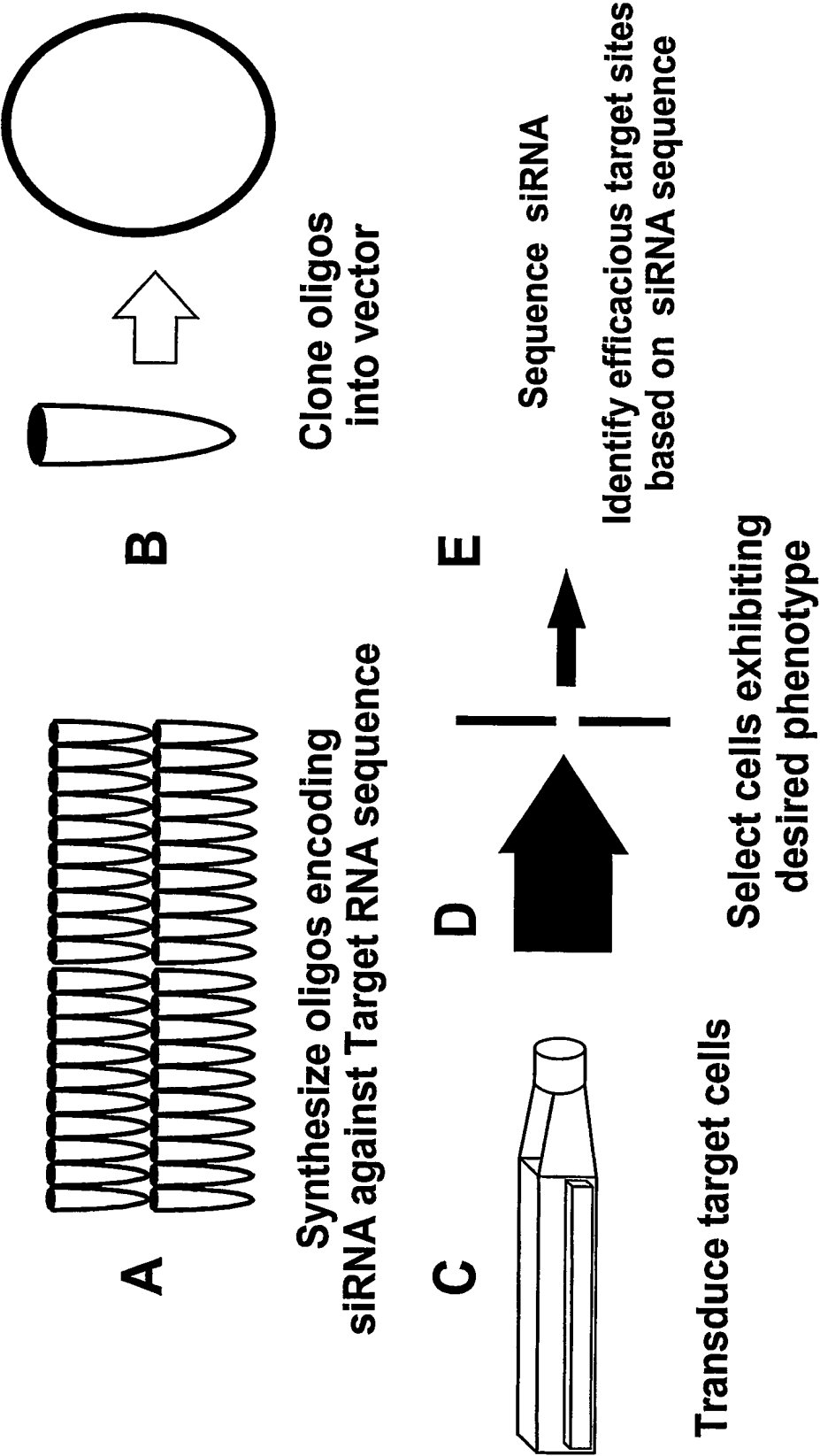
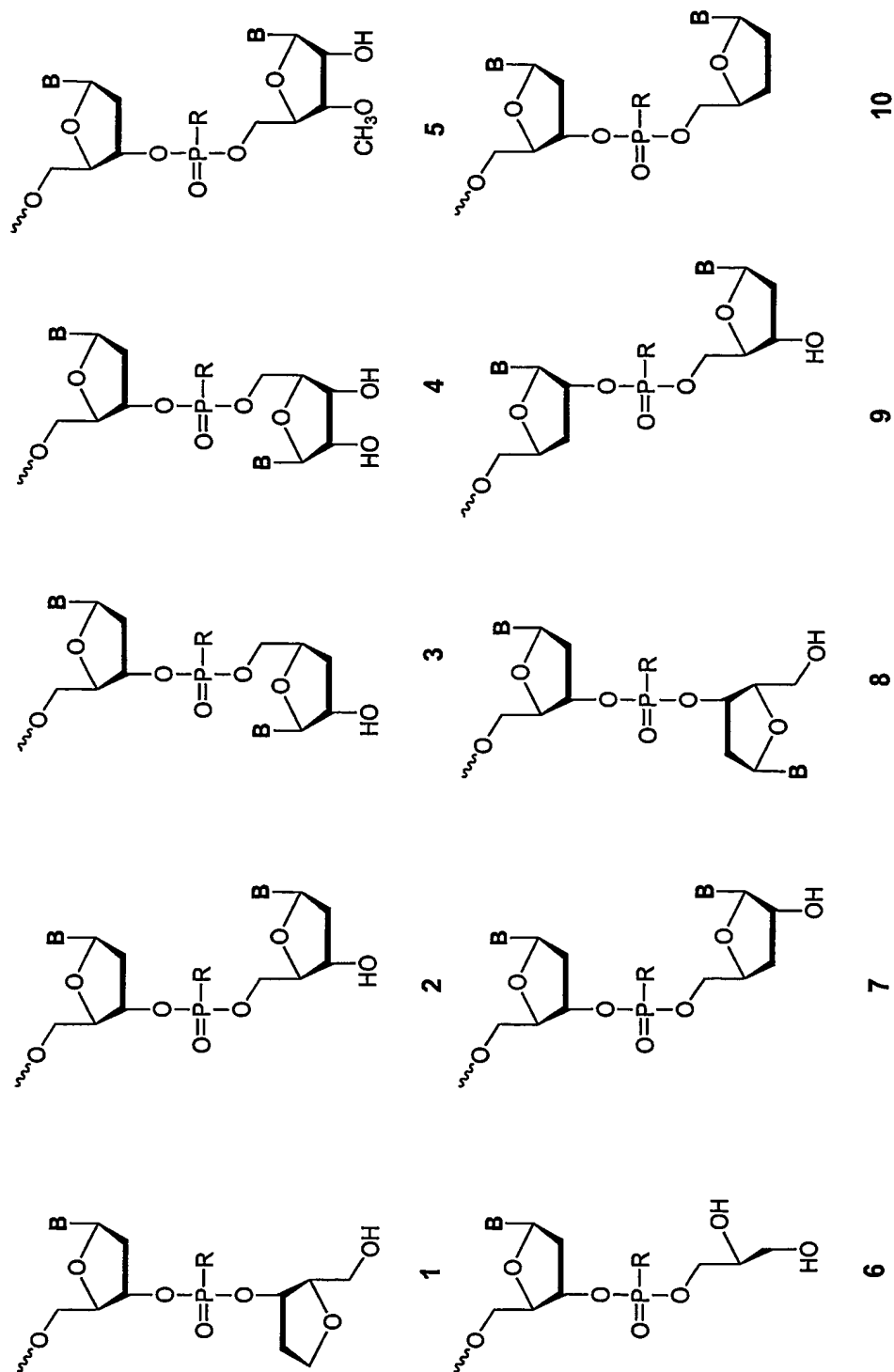


Figure 10

R = O, S, N, alkyl, substituted alkyl, O-alkyl, S-alkyl, alkaryl, or aralkyl

B = Independently any nucleotide base, either naturally occurring or chemically modified, or optionally H (abasic).

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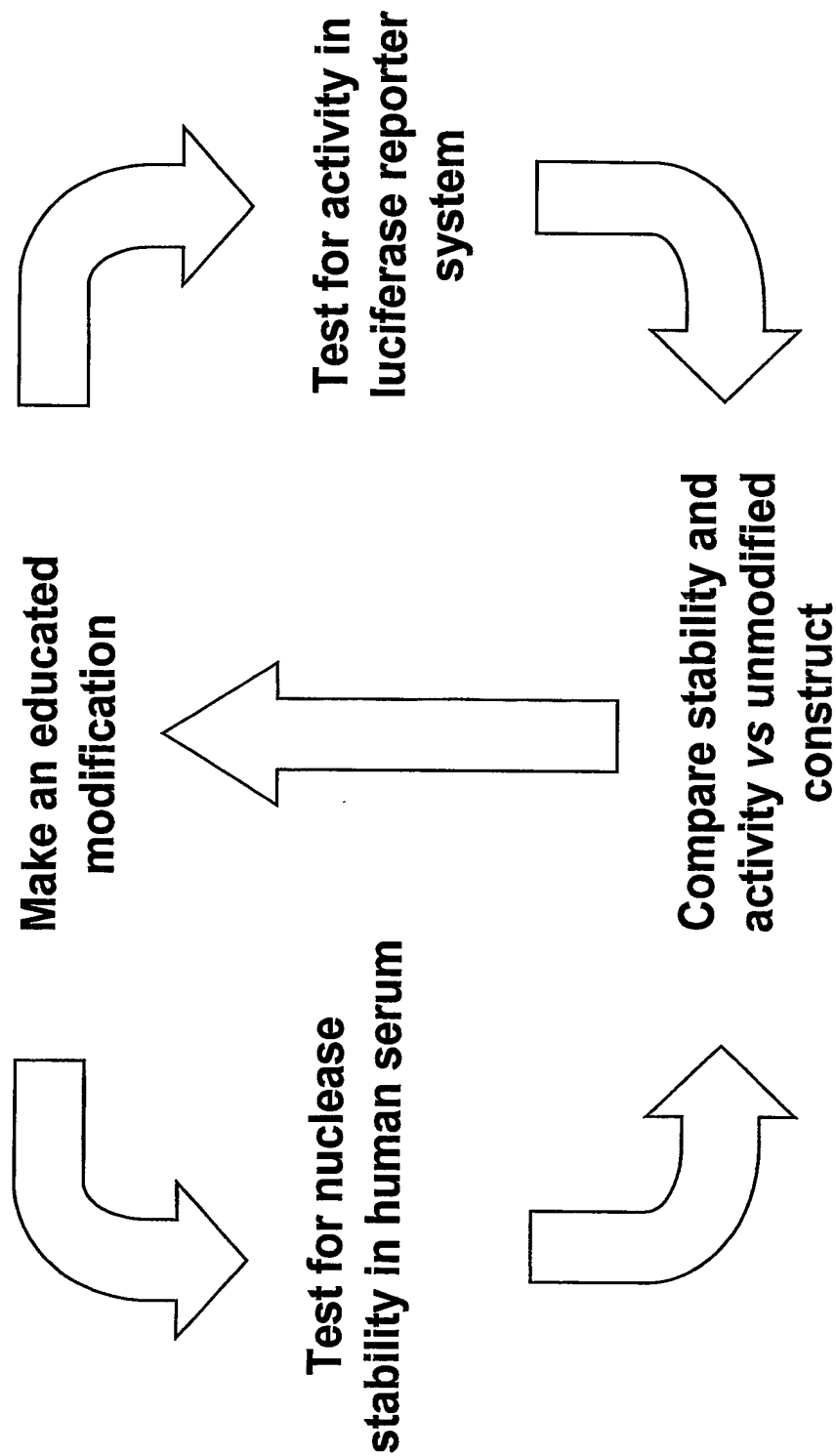
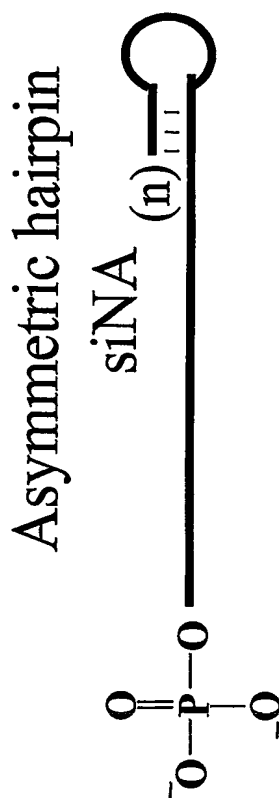
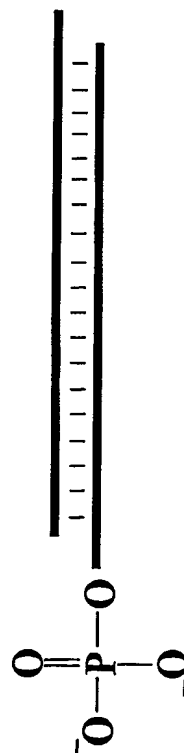
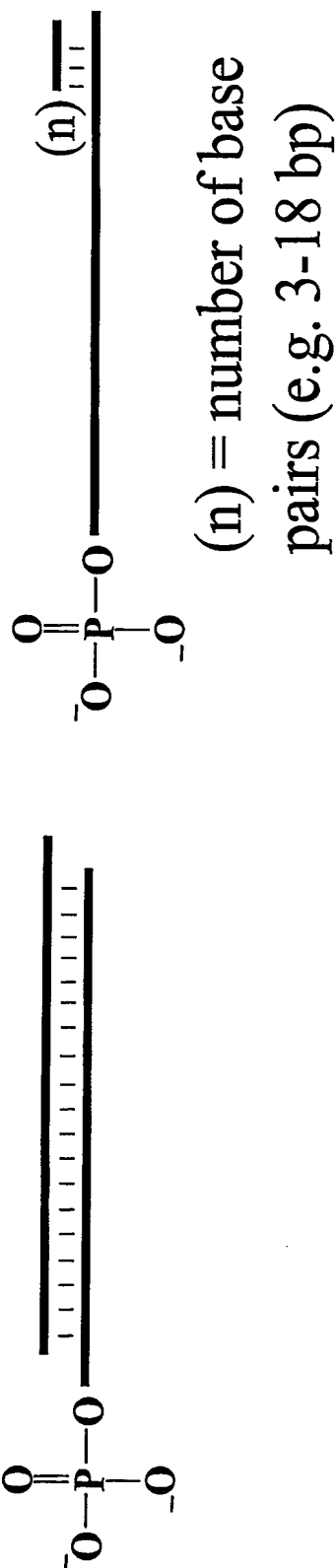
Figure 11: Modification Strategy

Figure 12: Phosphorylated siNA constructs

Phosphates can be modified
as described herein



Asymmetric duplex
siNA



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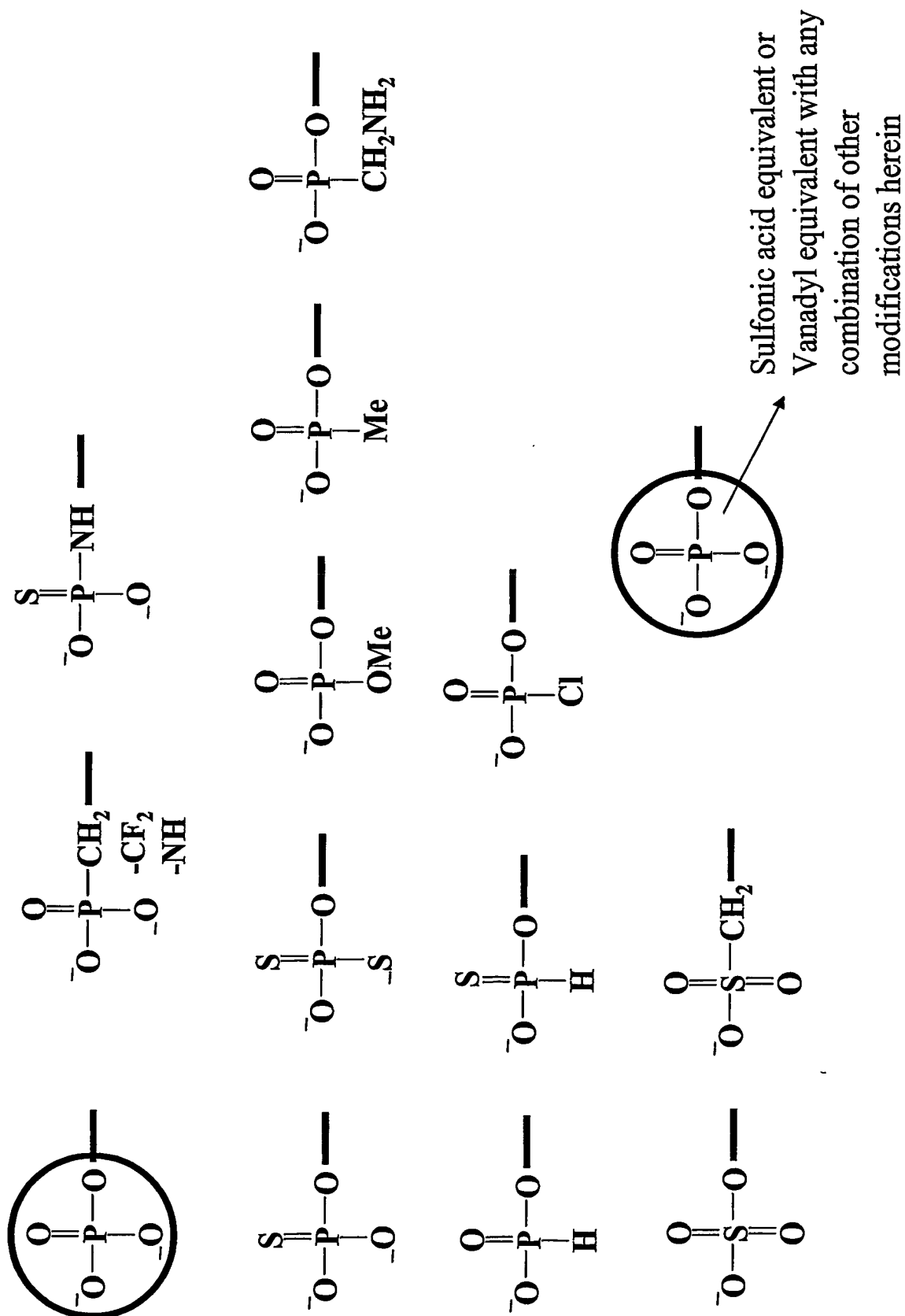
Figure 13: 5'-phosphate modifications

Figure 14A: Duplex forming oligonucleotide constructs that utilize Palindrome or repeat sequences

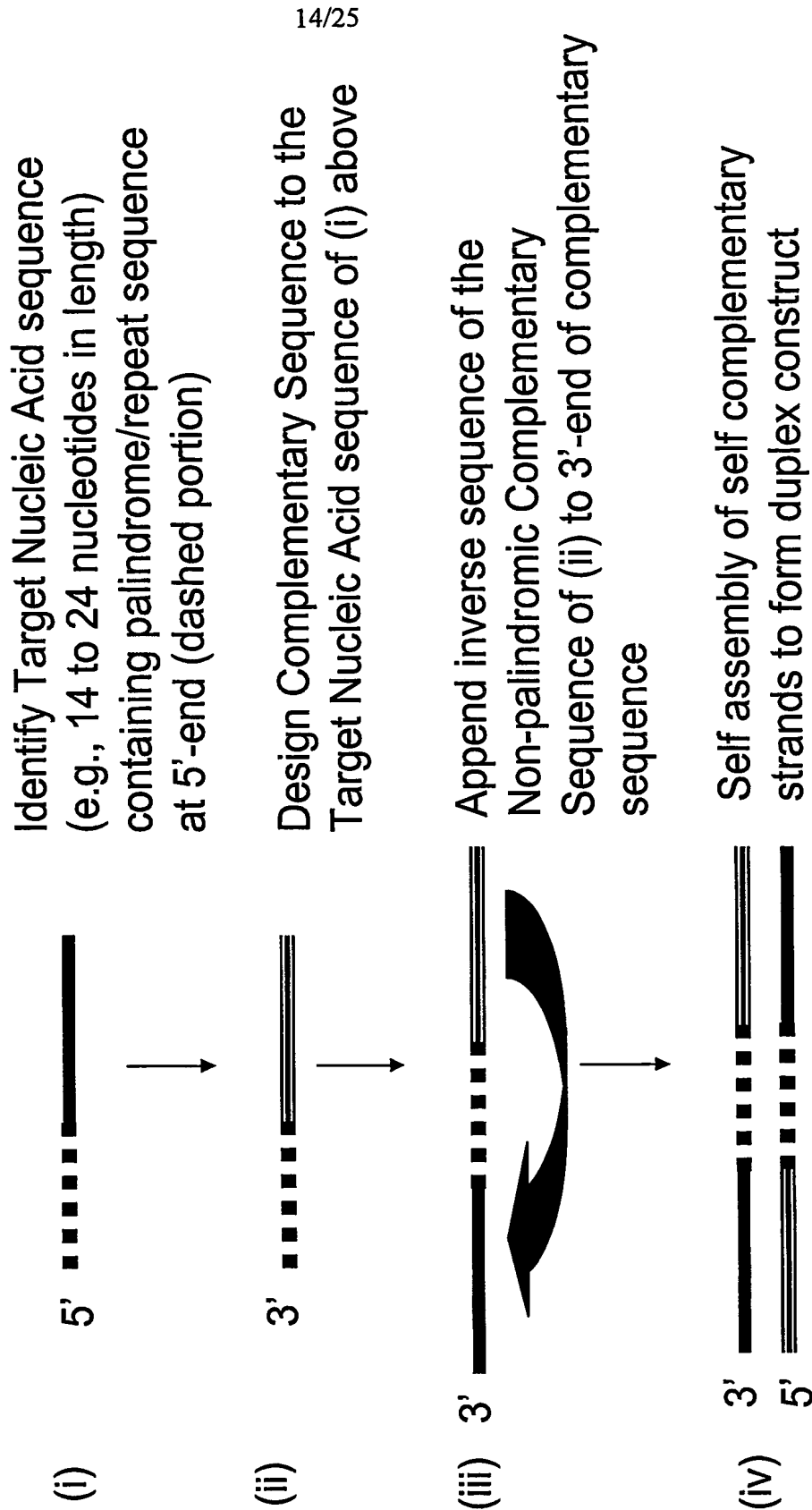


Figure 14B: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence

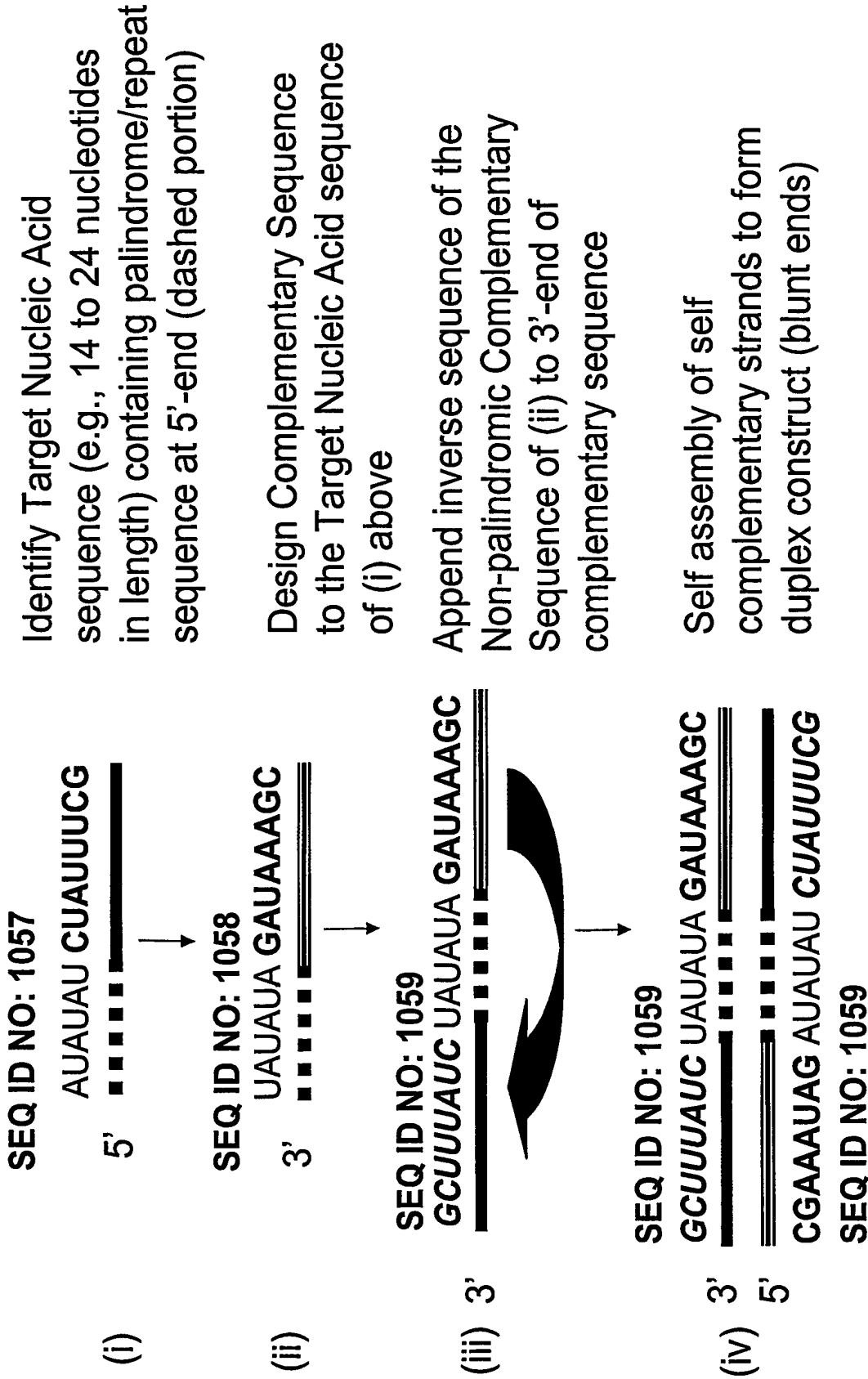
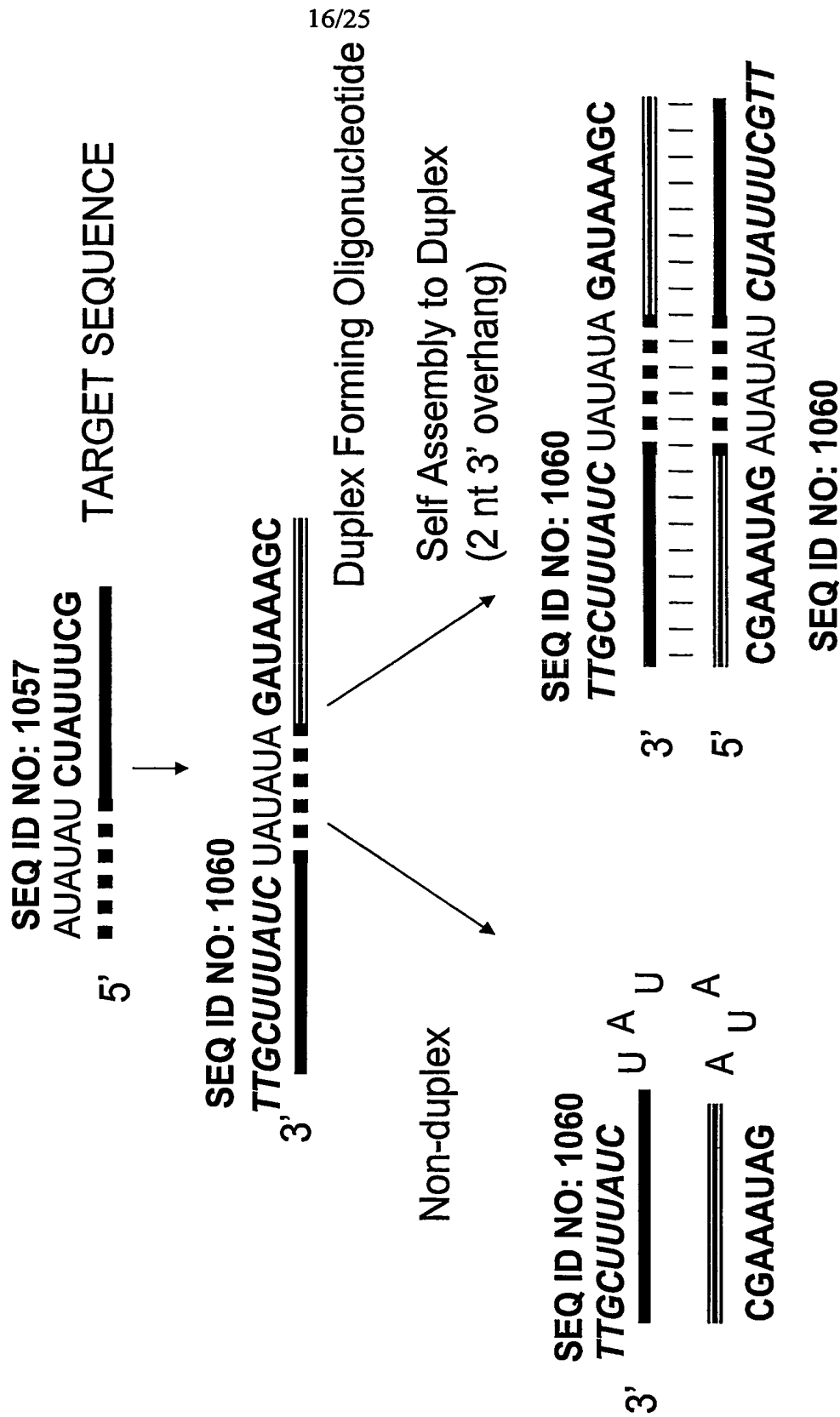


Figure 14C: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly



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Figure 14D: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly and inhibition of Target Sequence Expression

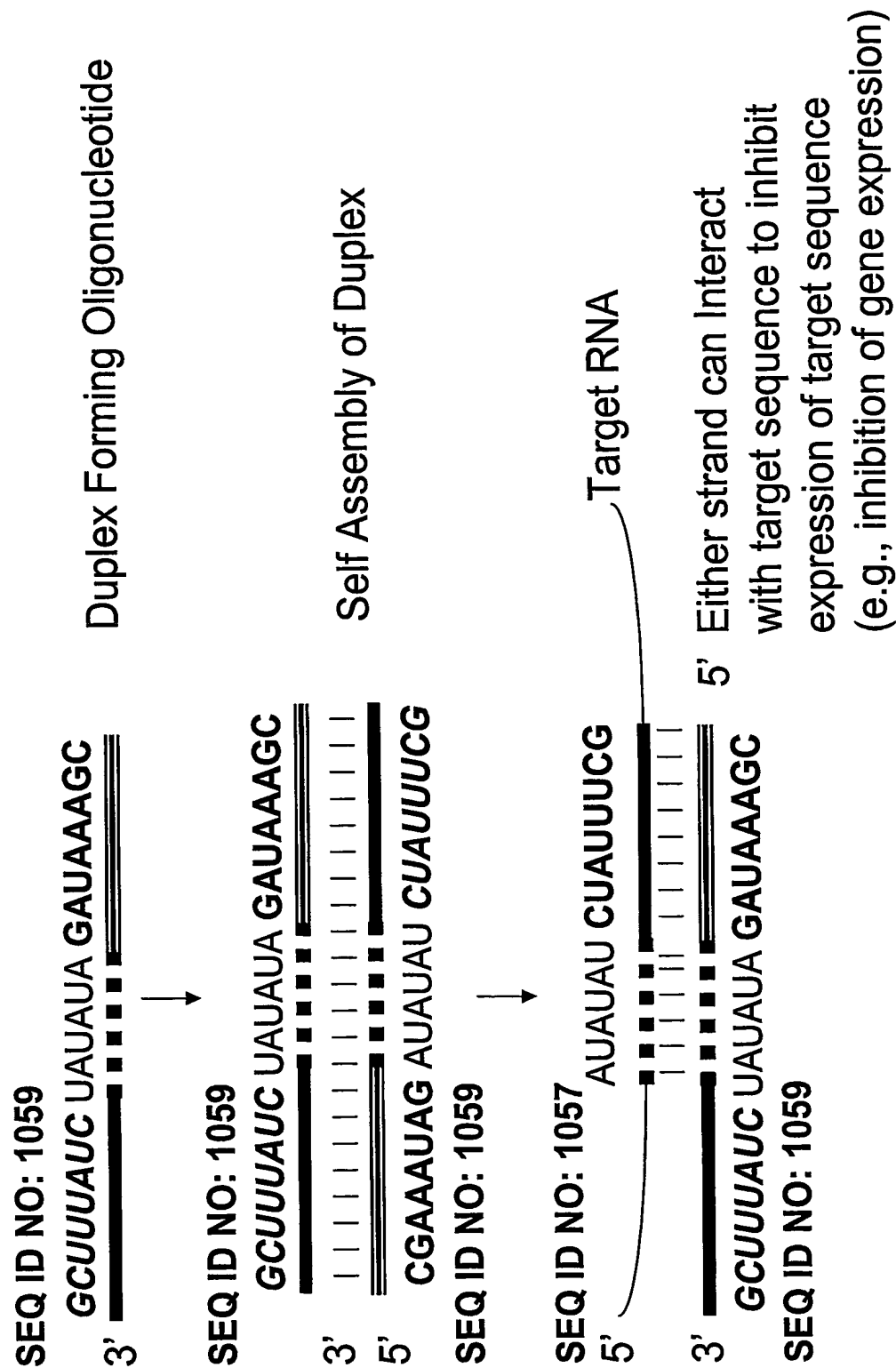


Figure 15: Duplex forming oligonucleotide constructs that utilize artificial palindrome or repeat sequences

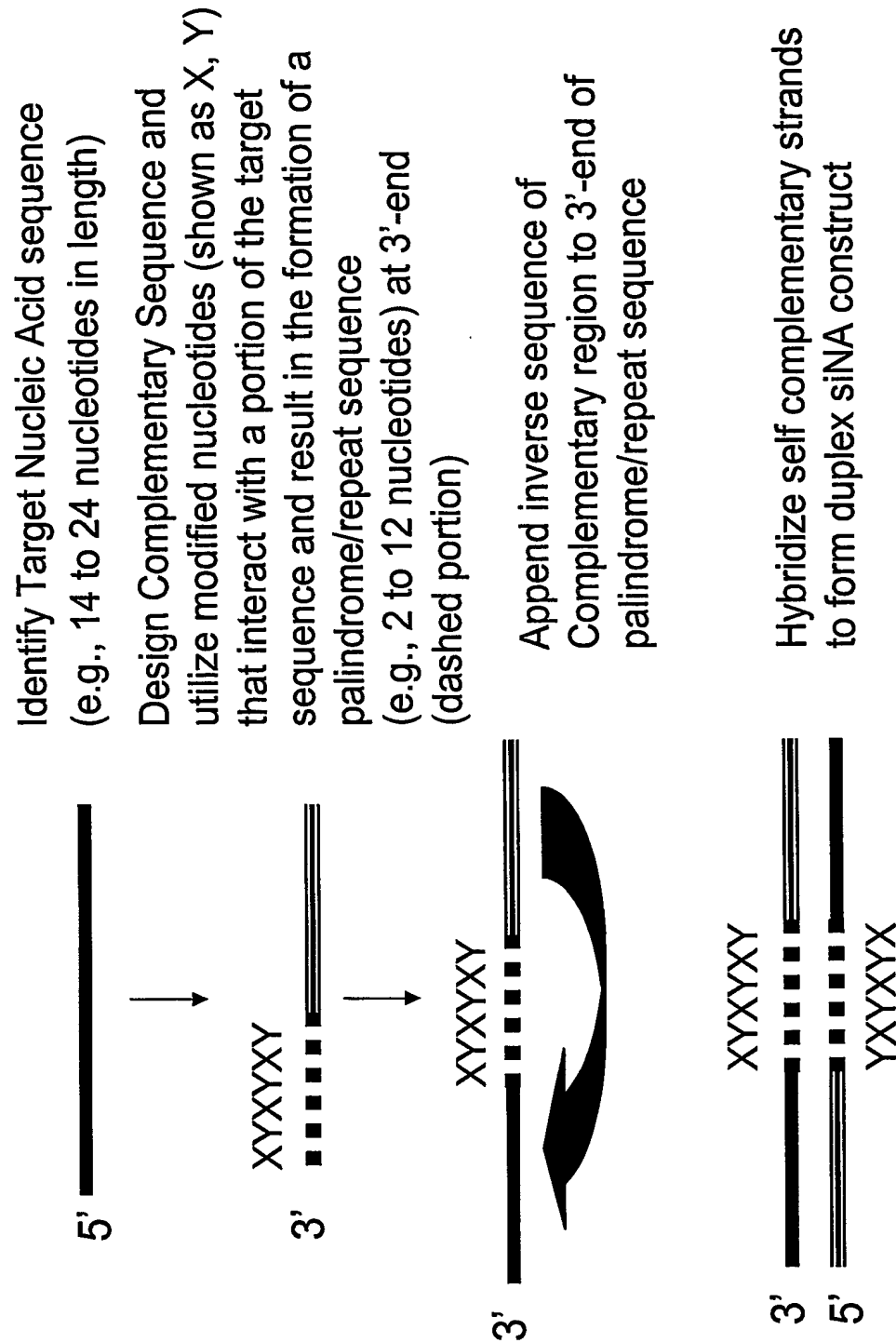
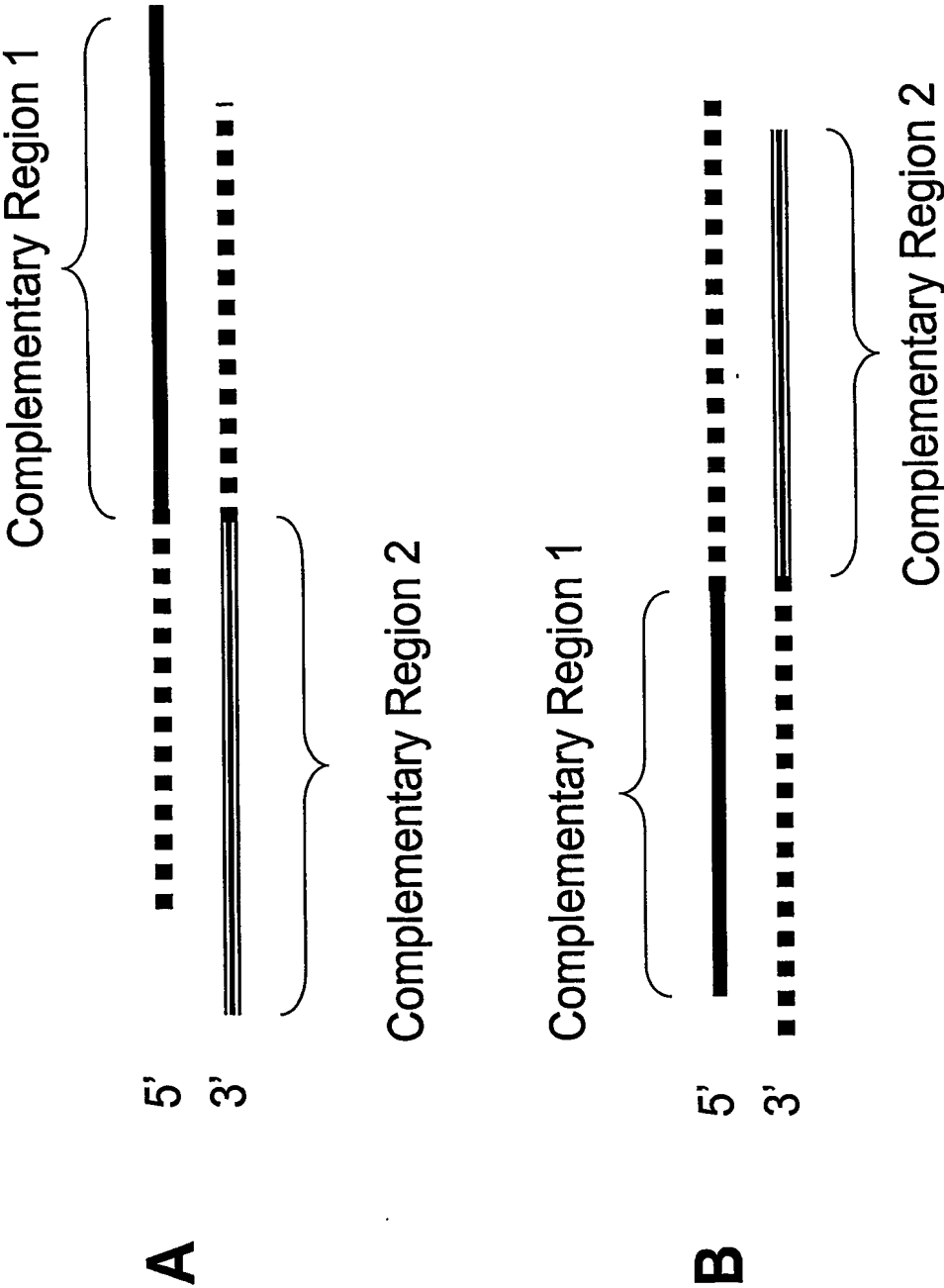


Figure 16: Examples of double stranded multifunctional siNA constructs with distinct complementary regions



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Figure 17: Examples of hairpin multifunctional siNA constructs with distinct complementary regions

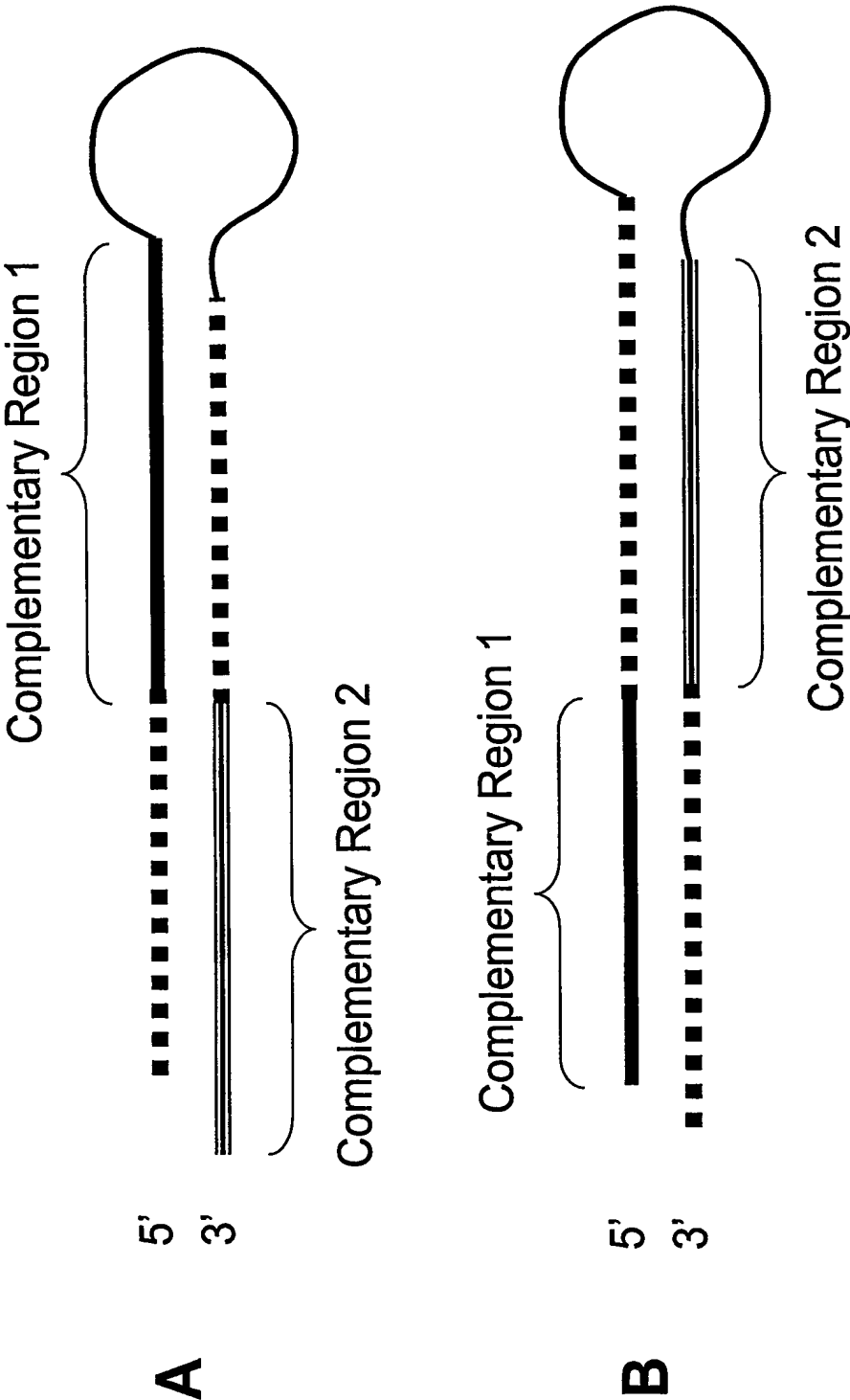


Figure 18: *Examples of double stranded multifunctional siNA constructs with distinct complementary regions and a self complementary/palindrome region*

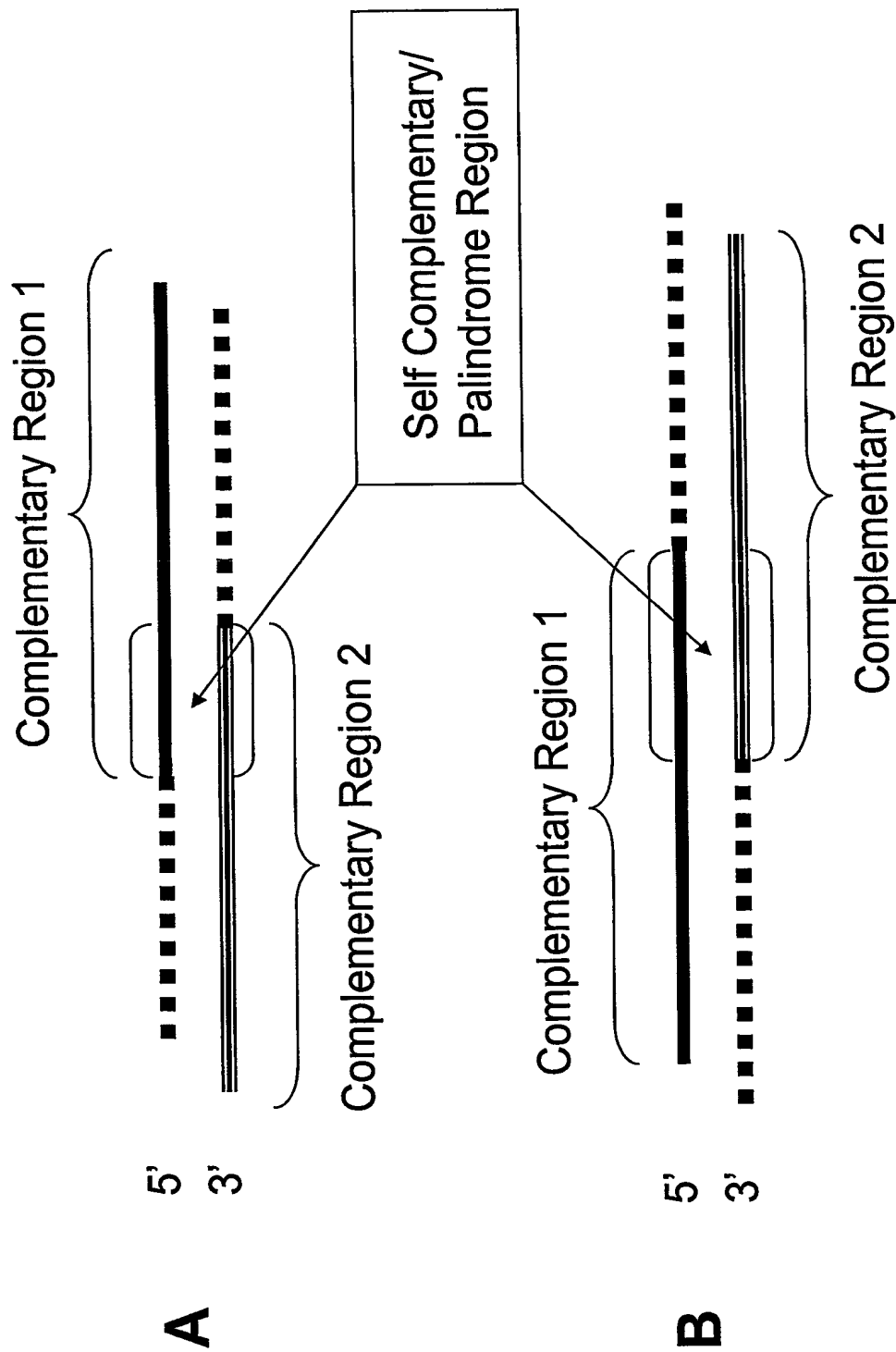
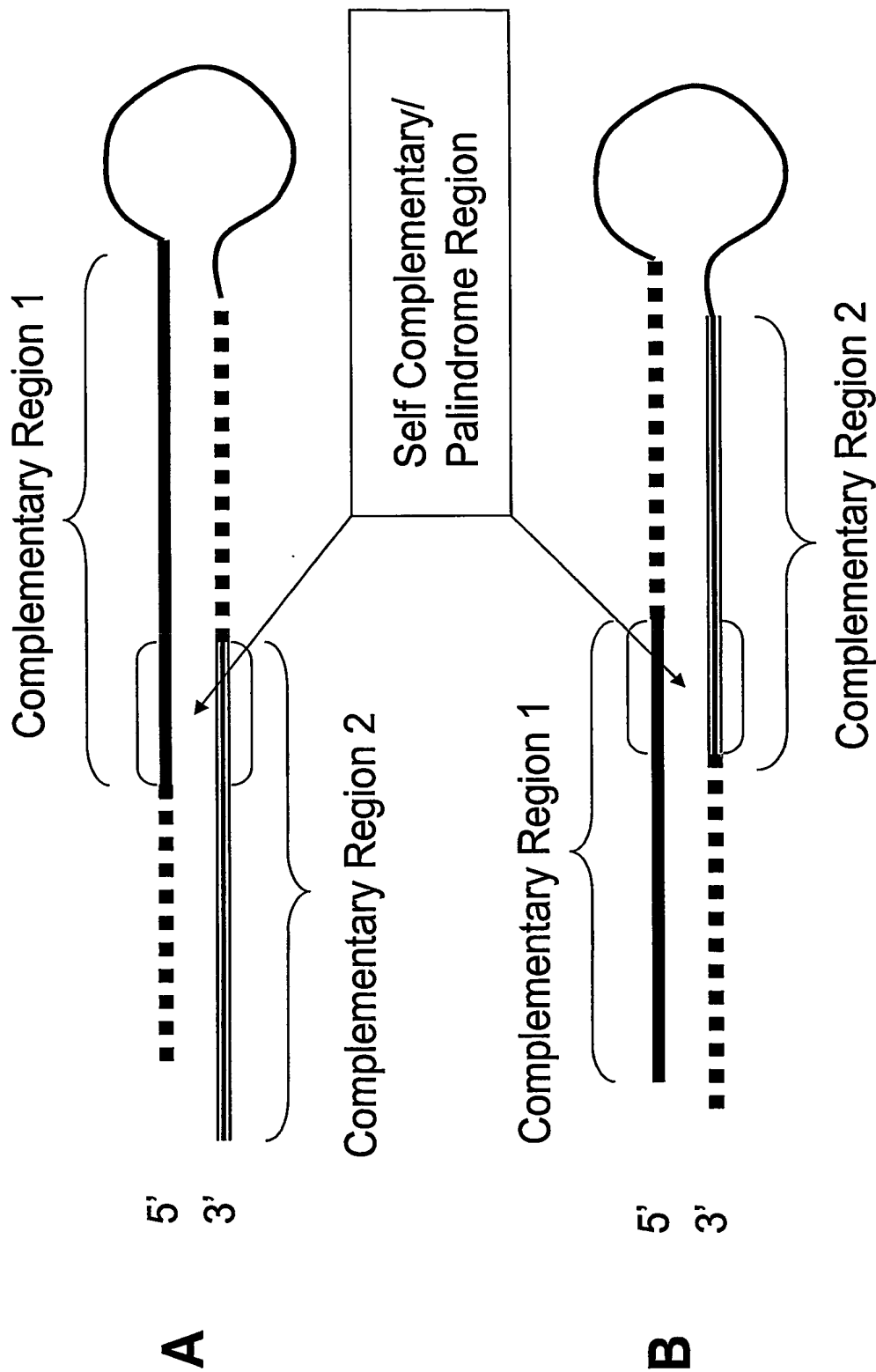


Figure 19: Examples of hairpin multifunctional siNA constructs with distinct complementary regions and a self complementary/palindrome region



**Figure 20: Example of multifunctional siNA targeting two
Separate Target nucleic acid sequences**

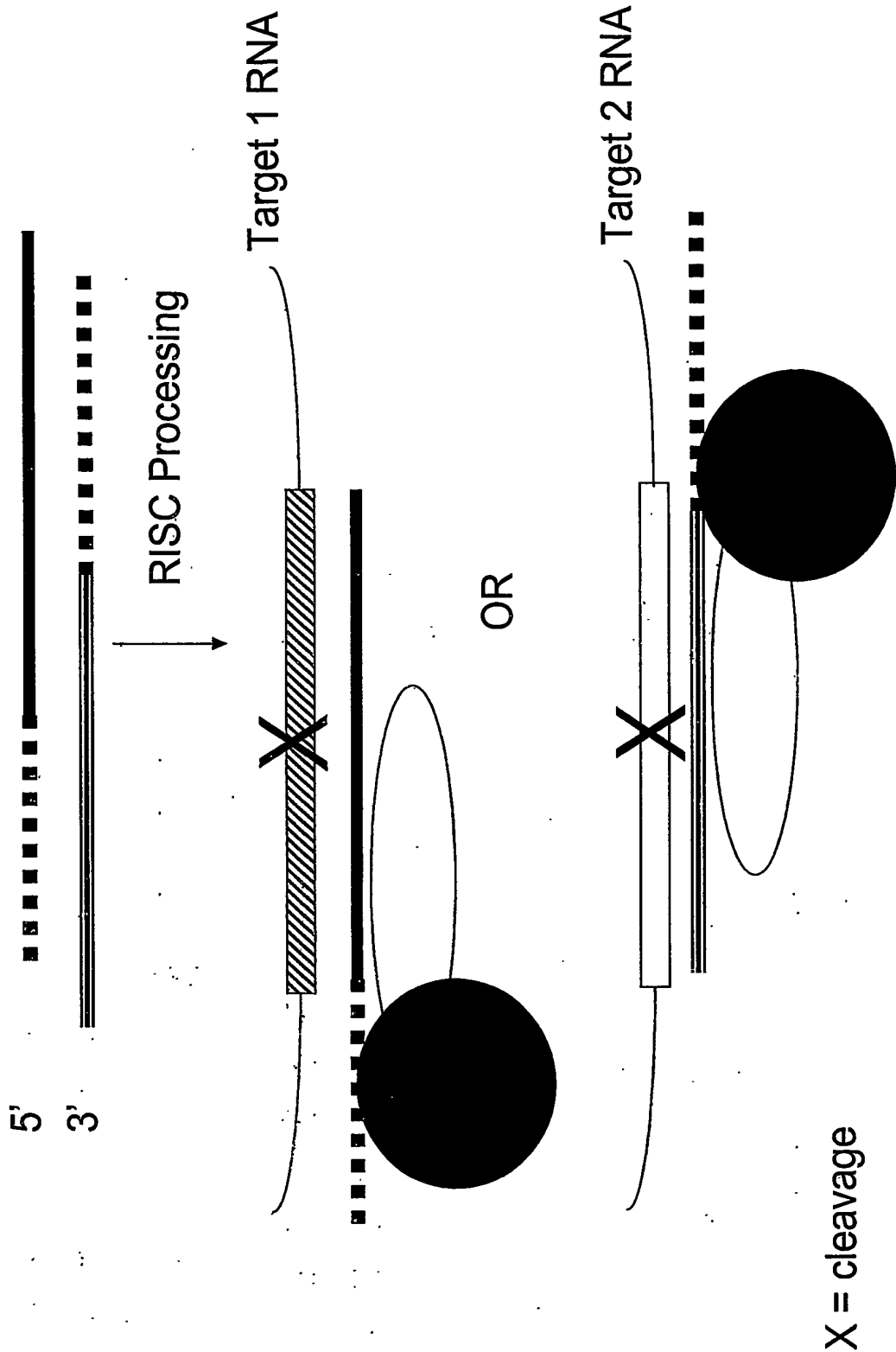


Figure 21: Example of multifunctional siNA targeting two regions within the same target nucleic acid sequence

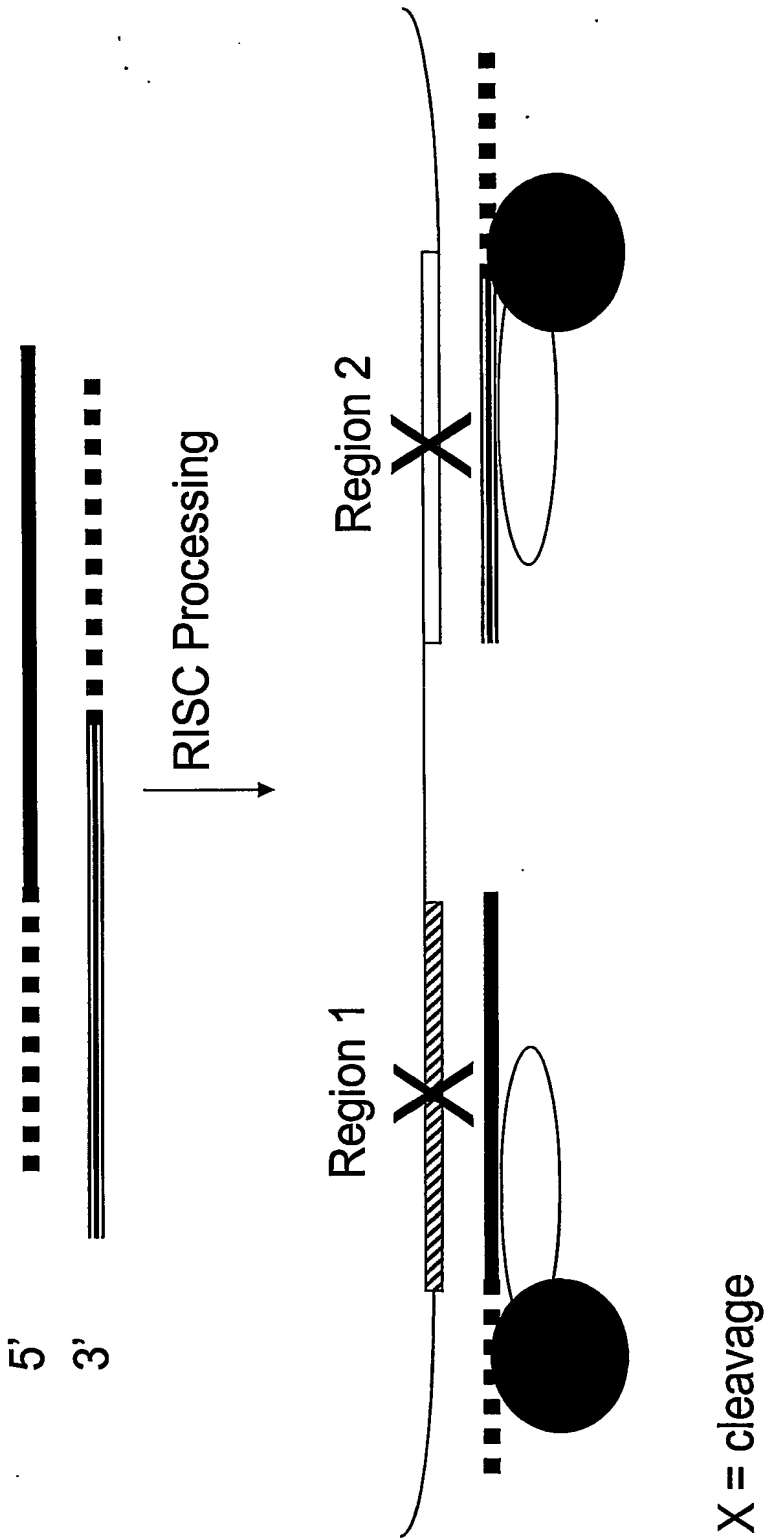
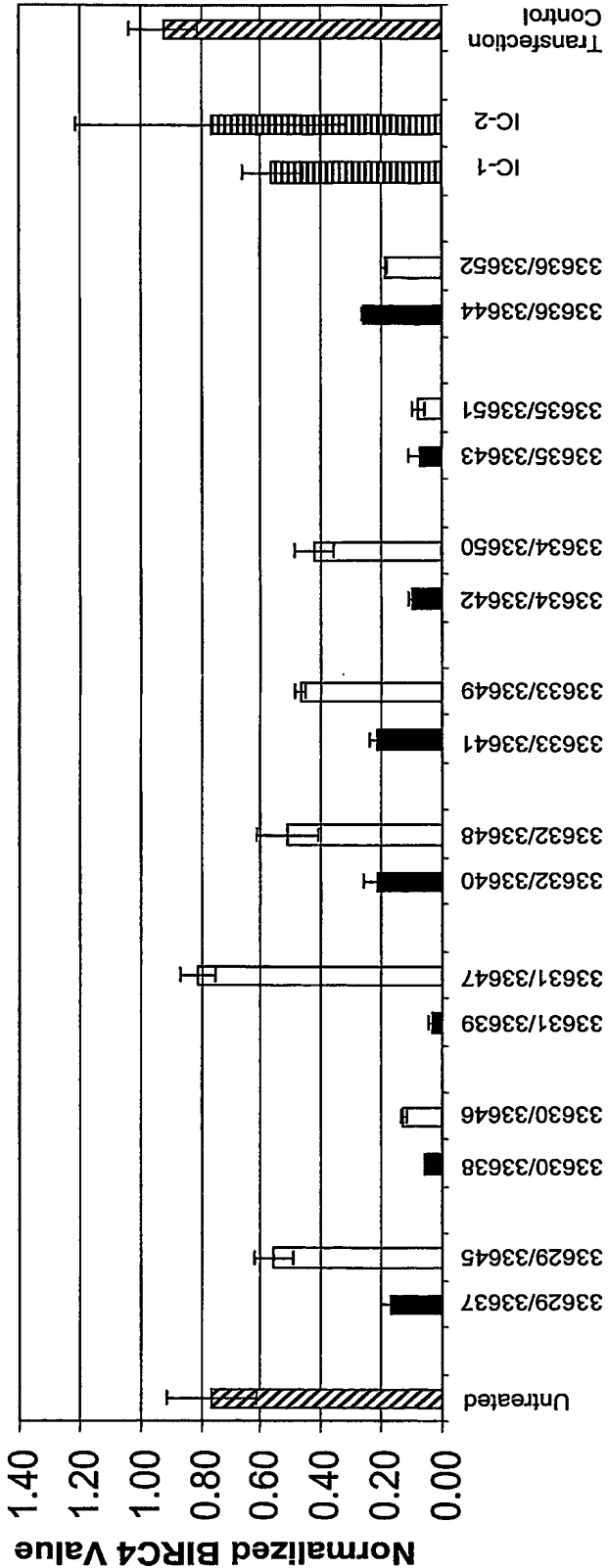


FIGURE 22

A549 24h BIRC4 mRNA Expression
0.25 µl/well LF2K Transfection
5,000 Cells/Well



25 nM Treatment